REMARKS/ARGUMENTS

Claim 1 is amended. Claims 3, 5, 8, 10, 15, 17, 19, 24, 26, 28, 33, 35, 36, 42, 45, 47,and 50-55 are cancelled without prejudice of disclaimer. Claims 1, 2, 4, 6, 7, 9, 11-14, 16, 18, 20-23, 25, 27, 29-32, 34, 37-41, 43, 44, 46, 48, 49 and 56-71 are pending.

Claim amendments

Claim 1 is amended to more specifically recite various preferred embodiments of the present invention. In particular, the preamble of claim 1 is amended to recite that the modified xylanase is a Family 11 xylanase. In addition, the claim is amended to specify that the modified Family 11 xylanase exhibits xylanase activity on a xylan substrate. Support for this amendment may be found, for example, on page 42, Example 2-3, which describes a standard assay for the measurement of enzymatic activity. Furthermore, claim 1 is amended to recite that the modified Family 11 xylanase is derived from a native Family 11 xylanase that has 48-100% sequence similarity to the *Trichoderma reesei* xylanase II amino acid sequence of SEQ ID NO:16. Support for this amendment may be found in Figure 1, which discloses the amino acid sequence alignment of 21 known native Family 11 xylanases which have between 48 and 100% sequence identity to SEQ ID NO:16 (Tr2 in Figure 1).

Rejection under USC 112, first paragraph

(i) Enablement

Claims 1, 2, 4-7, 9, 11-14, 16, 18, 20-23, 25, 27, 29-32, 34, 37-41, 43, 44, 46, 48, 49 and 56-71 stand rejected under 35 U.S.C.112, first paragraph as lacking enablement on the ground that the specification does not reasonably provide enablement for any modified xylanase comprising a non-polar amino acid at position 116, a Cys at position 118, a basic amino acid at position 144 and 161 wherein said positions correspond to the amino acid positions in SEQ ID NO:16.

In particular, Examiner alleges that the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of xylanases broadly encompassed by the claims. To support this assertion, Examiner contends that it would require undue experimentation of the skilled artisan to make and use all of the claimed polypeptides. In this regard, Examiner alleges that the specification is limited to

teaching the use of SEQ ID NO:16 as a parent xylanase wherein amino acids at specific positions are modified, but provides no guidance with regard to the making of any or all variants and mutants of SEQ ID NO:16. Examiner further alleges that "[t]he scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of xylanases broadly encompassed by the claims."

Respectfully submitted, the claims need not be limited to specific exemplified embodiments or technical examples disclosed in the specification. As explained in *Falko-Gunter Falkner, et al. v. Inglis, et al.*:

> A claim will not be invalidated on section 112 grounds simply because the embodiments of the specification do not contain examples explicitly covering the full scope of the claim language. That is because the patent specification is written for a person of skill in the art, and *such a person comes to the patent with knowledge of what has come before.* Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation. (Emphasis added).

Fed. Cir. 2006, 05-1324 (citing *Lizard Tech Inc. v. Earth Resource, PTY, Inc.* 424 F.3d 1335 (Fed.Cir. 2005)). In the present case, the person of ordinary skill in the art possesses significant knowledge and understanding of Family 11 xylanases. Applicant submits concurrently herewith a Declaration of Dr. Theresa White to provide clarification on what those of skill in the art would understand from the prior art concerning Family 11 xylanases at the time the present invention was made. As set forth in the Declaration, Family 11 xylanases have been extensively characterized and well-documented in the literature. For instance, numerous amino acid sequences of different Family 11 xylanases of bacterial and fungal origins have been published, for example as shown in Figure 1 of the application. All Family 11 xylanases, including those from species as diverse as bacteria and fungi, share the same general molecular structure comprising mainly beta-sheets, turns, a single alpha helix and two glutamate residues in their active site. Alignment of the amino acid sequences of numerous Family 11 xylanases identified highly conserved signature sequences in the beta-sheets as well as in the alpha helix. Furthermore, the three-dimensional structures of Family 11 xylanases

family members have been determined by X-ray crystallography, indicating only very small levels of deviation among the family members.

Moreover, cloning of Family 11 xylanases is now a routine matter to one of skill in the art, as evidenced by the numerous Family 11 xylanases that have been cloned. (see attached Declaration). The techniques used to construct modified xylanases are basic recombinant DNA methods such as oligo-nucleotide-mediated mutagenesis, error-prone polymerase chain reaction, restriction enzyme digestion, ligation, transformation, and DNA hybridization. Similarly, the activity assays used to identify modified xylanases that retain enzymatic activity (by release of reducing sugars from xylan subtrates or using commercial derivatized xylan substrates and methods such as those readily available from Megazyme International Ireland, Ltd) and to assess the temperature optima of xylanase enzymes are well-known from the published literature describing the discovery and characterization of naturally occurring Family 11 xylanases from diverse microbial sources. As set forth in the attached Declaration, these techniques fall within the purview of one of ordinary skill in the art. Furthermore, the attached Declaration sets forth specific techniques for cloning and producing enzyme variants that were known at the filing date of the present specification. Thus, it would be a routine matter for a person of ordinary skill in the art to prepare a modified Family 11 xylanase comprising one or more of the amino acid substitutions encompassed by the claims.

Given the extent of knowledge and understanding of Family 11 xylanases in the prior art, their high degree of homology among diverse species, coupled with the available techniques in which a person of skill in the art could apply basic protein engineering techniques to produce a modified Family 11 xylanase encompassed by the claims, Applicant submits that the claims are sufficiently enabled

With respect to Examiner's comment that an "extremely large number of xylanases [is] broadly encompassed by the claims," Applicant submits that the number of mutations that can be introduced into the amino acid sequence is limited in that claim 1 recites that the xylanase is a Family 11 xylanase that exhibits activity against a xylan substrate. These features significantly reduces the number of variants encompassed by the claims. Moreover, the claims encompass only those Family 11 xylanases derived from a native Family 11 xylanase that exhibit at least 48% sequence identity to SEQ ID NO:16 (which is calculated from the sequence similarity of those Family 11 xylanases disclosed in Figure 1 of the specification).

Additionally, conserved regions of Family 11 xylanases are well documented in the prior art (see the attached Declaration), and the specification particularly points out such regions among the Family 11 xylanases disclosed in Figure 1 (see bolded amino acids in Figure 1). It would be well-known by those of skill in the art that mutations at conserved positions are necessarily avoided in order to produce a variant with activity on a xylan substrate, as recited by each independent claim.

Examiner also contends that the claims continue to suffer from the enablement issues because "irrespective of whatever guidance is provided in the specification or in the art, one of ordinary skill in the art will be subject to undue experimentation in order to arrive at active polypeptides having thermophilic activity as claimed."

Applicant submits that, at the time of the invention, it was well within the ability of a person skilled in the art to produce modified enzymes with improved characteristics without necessarily having knowledge of the relationships between the sequence structure and function of the proteins.

Furthermore, the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. Indeed, great expenditures of time and effort are ordinary in the field of protein engineering. Moreover, a patent need not teach and preferably omits, what is well known in the art (*Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F 2d 1524, 1534 (Fed. Cir. 1987)). In the present case, screening methods are routine and thus guidance in the specification is not required.

In view of the above arguments, Applicant submits that claims 1, 2, 4-7, 9, 11-14, 16, 18, 20-23, 25, 27, 29-32, 34, 37-41, 43, 44, 46, 48, 49 and 56-71 are sufficiently enabled as required under 35 U.S.C. 112, first paragraph. Accordingly, removal of the rejection is respectfully requested.

(ii) Written Description

Claims 1, 2, 4-7, 9, 11-14, 16, 18, 20-23, 25, 27, 29-32, 34, 37-41, 43, 44, 46, 48, 49 and 56-71 stand rejected under 35 U.S.C.112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular, Examiner asserts that the "claims are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides derived from SEQ ID NO:16 including modified polypeptides sequences comprising specific substitutions...and other modifications that have not been disclosed in the specification." The Examiner further contends that "[n]o description has been provided for all the modified polypeptide sequences encompassed by the claim." Applicant respectfully traverses this rejection.

While it is correct that a generic invention requires adequate support, the sufficiency of written description support is a factual-based inquiry. See *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). In the present case, the claimed invention does not concern the discovery of a previously unknown Family 11 xylanase. Family 11 xylanases are a well-characterized group of enzymes and over 80 Family 11 xylanase amino acid sequences have been cloned and sequenced. (See attached Declaration). Rather, the invention concerns the introduction of mutations at specific positions in known amino acid sequences to enhance the thermophilicity of the enzymes, and thus their utility for certain applications such as pulp bleaching. Furthermore, given the abundance of knowledge and understanding of the enzymes, coupled with the level of the skill in the art, it would be a routine matter to prepare a Family 11 xylanase comprising one or more substituted amino acids at the positions specified in the claims using standard recombinant techniques.

Against this background, the recitation of known Family 11 xylanases comprising amino acid substitutions at the positions claimed is not required. (See, for example, *Capon v. Eshhar*, 418 F.3d 1349, 1360 (Fed. Cir. 2005)). Moreover, a patent need not teach and preferably omits, what is well known in the art (*Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987)). Applicant submits that recitation of known Family 11 xylanase amino acid sequences comprising amino acid substitutions at the positions claimed would unnecessarily add to the bulk of the description.

Examiner contends that "[t]he specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus." To support this assertion, Examiner states that "[t]he genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures". Examiner further alleges that "[t]herefore many structurally unrelated polypeptides are encompassed within the scope of these claims".

The attached Declaration provides clarification on what those of skill in the art would understand from the prior art concerning Family 11 xylanases at the time the present invention was made. As set forth in the attached Declaration, Family 11 xylanases are known as a homogeneous group of enzymes with highly conserved amino acid sequences and three-dimensional structures among species. As discussed previously in connection with enablement requirements, the amino acid sequences of Family 11 xylanases from species as diverse as bacteria and fungi share the same general molecular structure comprising mainly beta-sheets, turns and a single alpha helix and two conserved glutamate residues in their catalytic sites. Furthermore, the three-dimensional structures of Family 11 xylanases family members have been determined by X-ray crystallography, indicating only very small levels of deviation among the family members.

Accordingly, the examples provided in the specification of modified *Trichoderma reesei* xylanase II enzymes are sufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

Applicant submits that, in view of the above arguments, the subject matter of claims 1, 2, 4-7, 9, 11-14, 16, 18, 20-23, 25, 27, 29-32, 34, 37-41, 43, 44, 46, 48, 49 and 56-71 satisfy written description requirements under §35 USC 112. Accordingly, removal of the rejection is respectfully requested.

Claim Rejections – 35 USC 102

Examiner rejects claims 1, 2, 4, 9 and 48 under 35 U.S.C. 102(e) as being anticipated by Paloheimo et al. (U.S. Patent No. 6,228,629) or Van Ooigen et al. (U.S. Patent No. 5,610,046) or Hansen et al. (U.S. Patent No. 5,817,500).

In particular, Examiner alleges that Paloheimo et al. or Van Ooigen et al. disclose an identical xylanase which encompasses a variant comprising a substitution at positions 144, 161

with a basic amino acid, as determined by sequence alignment with SEQ ID NO:16. Examiner likewise rejects the claims under 35 U.S.C. 102(e) as being anticipated by Hansen et al., alleging that Hansen et al. disclose an identical xylanase which encompasses a variant comprising a substitution at positions 144, 161 with a basic amino acid, a Lysine and an Arg, an Asp in position 11, and Gly as the non-polar amino acid at position 118.

Examiner also contends that although the references may not explicitly state that the thermophilicity of the modified xylanase was improved over the native xylanase, because the referenced xylanases comprise the very same mutation that is being claimed, Examiner takes the position that the functional characteristic is an inherent characteristic of the modified xylanases.

As Examiner is aware, the present invention as recited in the independent claims relates to a *modified* Family 11 xylanase having improved thermophilicity relative to a corresponding native Family 11 xylanase. The Family 11 xylanase is modified by introducing one or more amino acid *substitutions* at the positions specified.

None of the prior art cited by Examiner discloses a *modified* Family 11 xylanase. Rather, the sequences disclosed are wild-type sequences. In particular, van Ooyen et al. discloses wild-type amino acid sequences of *Aspergillus tubigensis* xynB, Paloheimo et al. discloses novel wild-type xylanases from *Chaetonium thermophilum* and Hansen et al. discloses wild-type amino acid sequences from *Thermomyces lanuginosus*. There is no teaching or suggestion of introducing one or more amino acid substitutions to produce a modified Family 11 xylanase with improved thermophilicity as claimed. Accordingly, claims 1, 2, 4, 9 and 48 are not anticipated under 35 U.S.C. 102(e) and removal of the rejection is respectfully requested.

Double Patenting

Examiner rejects claims 1, 2, 4, 9 and 48 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2, 4-6, 34-42 of U.S. Application No. 11/377,644.

As set forth in the previous Office Action response, Applicant will submit a terminal disclaimer in compliance with 37 CFR 1.321(c) with respect to commonly owned U.S. Application No. 11/377,644 when there has been an indication of allowable subject matter.

Conclusion

It is respectfully submitted that the above-identified application is now in a condition for allowance and favorable reconsideration and prompt allowance of these claims is respectfully requested. Should the Examiner believe that anything further is desirable in order to place the application in better condition for allowance, the Examiner is invited to contact the Applicant's undersigned attorney at the telephone number listed below.

If there are any fees due in connection with the filing of this amendment, please charge the fees to our Deposit Account No. **50-1283**. If a fee is required for an extension of time under 37 C.F.R. § 1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: 6/21/2007

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